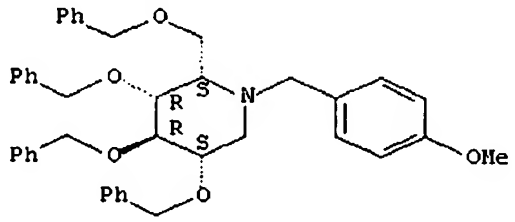
REMARKS

Claims 1-4, 6, 7 and 23-38 are pending in the current application. Claims 5 and 8-22 were previously cancelled. Claims 7 and 24-38 were withdrawn for directing to non-elected subject matter. Claims 1-4, 6 and 23 have been rejected. Claim 23 has currently been cancelled.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 1-4 are directed to a compound of Formula I, claim 6 is directed to a composition comprising the compound of Formula I and claim 23 is directed to a compound of Formula III. The Examiner maintained the rejection of claims 1-4, 6 and 23 under 35 U.S.C. § 103(a) as being allegedly obvious in view of WO 02/055498 (hereinafter "WO '498"). The Examiner maintained that the compound of Example 15 on page 26 of WO '498:



is the closest art. The Examiner admitted that "[i]t is not the intention of WO '498 to use compound of Example 15 as a biologically active compound", *Final Office Action* dated 7/30/2010, page 4, but maintained that when absent the protecting group, said compound contains the free hydroxy, which would render the claimed invention obvious.

Without agreeing as to the accuracy of the Examiner's arguments, Applicants cancelled claim 23 for purposes of expediting prosecution and allowance of the claims.

With respect to claims 1-4 and claim 6, Applicants respectfully disagree with the Examiner. Comparing the compounds of claims 1-4 of the current invention to Example 15 of WO '498, there are two points of differences: (1) the R group of Example 15 is a methoxybenzyl while the R group of the currently claimed compounds is a C_{4-5}alkoxyphenylmethyl; and (2) the piperidine ring of Example 15 is substituted with benzyloxy groups while the currently claimed compounds are substituted with free hydroxy groups. To start from Example 15 of WO '498 and arrive at the claimed compounds of the invention would require one skilled in the art to take three steps, none of which are taught or suggested in the art so as to render obvious the claimed invention.

The first step one skilled in the art would need to take would be to deprotect the compound of Example 15 as WO '498 discloses that Example 15 is a "protected intermediate". Page 6, lines 23-26 of WO' 498 teaches that "when P is CH_2Ph the deprotection is conducted in the presence of hydrogen gas and a catalyst such as $PdCl_2$ or palladium on carbon in a suitable solvent . . . It will be understood that when P is CH_2Ph and R is CH_2Ph[,] the R group can also be removed under these conditions" so as to yield a partially de-benzylated compound or a fully de-benzylated compound of formula (II), i.e., an unsubstituted 2-hydroxymethyl-3,4,5-piperidinetriol. Applicants therefore respectfully submit that when the compound of Example 15 is deprotected as described, the resulting compound is an unsubstituted 2-hydroxymethyl-3,4,5-piperidinetriol (i.e., a compound of Formula II of WO '498) useful as an intermediate for the synthesis of various compounds disclosed in WO '498, not the lead compound of the reference.

Upon obtaining this unsubstituted 2-hydroxymethyl-3,4,5-piperidinetriol (i.e., a compound of Formula II of WO '498), one skilled in the art would then be required to decide which compound is most likely to succeed (i.e., identify the lead compound). Upon identification of the lead compound, one skilled in the art would finally be required to decide what modifications to make to the existing lead compound so as to improve upon it and arrive at the claimed invention.

All of the compounds exemplified in WO '498 are piperidine compounds substituted at the nitrogen atom with either an alkyl or unsubstituted phenylalkyl group. Table 2 of WO '498 shows that the compounds of Examples 2 and 3 (wherein R is n-butyl and n-pentyl respectively) have an IC_{50} of 10.6μM and 4.0μM respectively. In looking at WO '498, one skilled in the art would not be motivated to make alkoxybenzyl analogs as there is nothing in the art suggesting that these compounds would be better than the n-butyl or n-pentyl analogs of Example 2 and 3. The compounds of Examples 1 and 2 of the currently claimed invention (wherein R is pentyloxybenzyl and butoxybenzyl respectively), on the other hand, have an IC_{50} of 0.15μM and 0.42μM respectively against GCS. Nothing in WO '498 suggests that substituting the piperidine ring with a 4-(C_{4-5}alkoxy)-benzyl at the nitrogen atom in place of the n-butyl or n-pentyl would give a 10-70 fold increase in GCS activities. These properties are clearly unexpected and pursing compounds wherein R is C_{4-5}alkoxybenzyl (i.e., the claimed compound) is clearly unobvious.

The Examiner argued that the intended purpose of the compounds is irrelevant, citing to MPEP §§ 2112-2112.02. MPEP § 2112, however, pertains to rejection based on inherency. MPEP 2112.01 states that "if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present". However, the currently claimed compounds of Formula I are not identical to the intermediate Compound of Example 15 (neither are they identical to the deprotected compound of Example 15 nor any of the compounds disclosed in WO '498) and there is nothing inherent about the claimed compounds or their properties at all. To the point of inherent properties of intermediate compounds, MPEP § 2144.09, Subsection VI specifically states that "if prior art compounds have no utility, or utility only as intermediates, claimed structurally similar compounds may not be *prima facie* obvious over the prior art.". *Id.* (emphasis added). In addition, there are numerous cases wherein the Federal Circuit considered utility or properties (or lack thereof) of prior art compounds to be relevant in the determination of non-obviousness. *See In re Lalu*, 747 F.2d 703, 707 (Fed. Cir. 1984) ("a relevant property of a compound cannot be ignored in the determination of non-obviousness"). *See also Ortho-McNeil Pharma., Inc. v. Mylan Lab., Inc.*, 520 F.3d 1358 (Fed. Cir. 2008) (found nonobviousness where the claimed anti-convulsive compound was synthesized as an intermediate for an antidiatetic drug and wherein "the ordinary artisan in this field would have had to (at the time of invention without any clue of potential utility of the active ingredient) stop at that intermediate and test it for properties far afield from the purpose for the development in the first place (epilepsy rather than diabetes)."). *Id.* at p. 1364.

Here, it is clear that Example 15 is intended to be an intermediate with no specific biological activities disclosed. This difference in utility between Example 15 and the claimed compounds of Formula I is pertinent to the non-obviousness analysis. While WO '498 allows R to be, among many others, a C_{1-10}alkylaryl wherein aryl may be, among others, phenyl, wherein phenyl may be optionally substituted with, among many others, OR^1 wherein R^1 may be a C_{1-6}alkyl (i.e., generically discloses the currently claimed compound), it is established that a disclosure of a generic formula does not by itself render obvious a species of that genus. *See In re Baird*, 16 F.3d 380, 382 (Fed. Cir. Jan. 19, 1994) ('The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious.")(citing *In re Jones*, 958 F.2d 347, 350 (Fed. Cir. 1992). There is nothing in the art that suggests that, of all the possible substituents, that the C_{4-5}alkoxy substituent on the N1-benzyl is

preferred, rendering the selection of the claimed compound obvious. To go from Example 15 to the claimed compounds of Formula I, one skilled in the art would need to (1) deprotect Compound 15 to obtain an unsubstituted intermediate 2-hydroxymethyl-3,4,5-piperidinetriol (i.e., Compound of Formula II); then going against the teaching of WO '498 which specifically discloses and claims alkyl-substituted and unsubstituted arylalkyl-substituted piperidinetriol compounds, (2) reattach the cleaved methoxy-benzyl substituent to the nitrogen atom of the piperidinetriol; and without any particular reason or motivation (3) modify the methoxy group on the benzyl substituent so as to specifically make a C_{4-5}alkoxy group as currently claimed in the current application. Wherein the claimed compounds of the invention are three steps removed from the compound that is arguably the closest art. Applicants respectfully submit that there is nothing obvious about the claimed compounds at all. Reconsideration and withdrawal of the rejections of claims 1-4 and claim 6 is earnestly requested.

This response is filed within three months from the date of the mailing of the final office action dated July 30, 2010, which response is due October 30, 2010, it is believed this response is timely and no fees are required. If this is not correct, however, please charge any additional fees, or credit any overpayment, to Deposit Account No. 50-4255.

Respectfully submitted,

Dated: Sept. 13, 2010

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